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The polycystic kidney disease-1 protein, polycystin-1, binds and activates heterotrimeric G-proteins in vitro.

Parnell SC, Magenheimer BS, Maser RL, Rankin CA, Smine A, Okamoto T, Calvet JP.

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Analysis of the C-terminal cytosolic domain of human and mouse polycystin-1 has identified a number of conserved protein motifs, including a 20-amino-acid heterotrimeric G-protein activation sequence. A peptide specific for this sequence was synthesized and shown to activate purified bovine brain heterotrimeric Gi/Go in vitro. To test whether the C-terminal cytosolic domain of polycystin-1 stably binds G-proteins, GST-fusion constructs were used in pull-down and co-immunoprecipitation assays with purified bovine brain Gi/Go and rat brain lysates. This identified a 74-amino-acid minimal binding domain that includes the G-protein activation sequence. This region of polycystin-1, including the G-protein activation peptide and flanking amino acid sequences, is highly conserved in mouse, human, and puffer fish, lending further support to the functional importance of the minimal binding domain. These results suggest that polycystin-1 may function as a heterotrimeric G-protein coupled receptor. Copyright 1998 Academic Press.

PMID: 9792824 [PubMed - indexed for MEDLINE]

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Characterization and cell distribution of polycystin, the product of autosomal dominant polycystic kidney disease gene 1.

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BACKGROUND: In a majority of cases, autosomal dominant polycystic kidney disease (ADPKD) is caused by mutations within a putative open reading frame of the PKD1 gene. The encoded protein, polycystin, is predicted to span the plasma membrane several times and contains extracellular domains, suggestive of a role in cell adhesion. The cellular distribution and function of polycystin is not known. **MATERIALS AND METHODS:** We selected as immunogens two conserved 15 amino acid peptides: P1, located in a predicted extracellular region of polycystin, and P2, located in the C-terminal putative cytoplasmic tail. The anti-peptide antibodies from immunized rabbits were affinity purified on peptide-coupled resins and their specificity confirmed by their selective binding to recombinant polycystin fusion proteins. Western blotting and immunohistochemistry were used to characterize the size, tissue, and cell distribution of polycystin. **RESULTS:** A high-molecular mass protein (about 642 kD) was detected by Western blotting in rat brain tissue. A few additional bands, in the 100- to 400-kD range, probably representing tissue-specific variants and/or proteolytic fragments, were recognized in human and rat tissues. Polycystin was abundantly expressed in fetal kidney epithelia, where it displayed basolateral and apical membrane distribution in epithelial cells of the ureteric buds, collecting ducts, and glomeruli. In normal human adult kidney, polycystin was detected at moderate levels and in a cell surface-associated distribution in cortical collecting ducts and glomerular visceral epithelium. Expression of polycystin was significantly increased in cyst-lining epithelium in ADPKD kidneys, but was primarily intracellular. **CONCLUSIONS:** Polycystin appears to be a developmentally regulated and membrane-associated glycoprotein. Its intracellular localization in the cyst-lining epithelium of ADPKD kidneys suggests an abnormality in protein sorting in this disease.

PMID: 8972485 [PubMed - indexed for MEDLINE]